

REMARKS

I. Status of Claims

Upon entry of the present amendment, claims 4-6 and 8-31 will be pending in this application. Claim 24 is presently amended; claims 4-6 and 8-23 are withdrawn by the Examiner as drawn to a non-elected invention; and claims 25-31 are newly added. Support for the amended and new claims can be found, e.g., at page 6, lines 12-13 and lines 25-26; the paragraph bridging pages 6-7; and page 7, lines 13-18, of the substitute specification filed September 28, 2006.

If the Examiner decides to withdraw any of the new claims from the presently examined group, Applicants request that they be rejoined once the claims under examination are found to be allowable.

II. Rejections Under 35 U.S.C. § 103(a)

(a) Claim 24 is rejected as allegedly being obvious over Sugiyama et al. (US 6,225,051 B1) in view of Ast et al. (*Nucleic Acids Res.*, 25:3508-3513 (1997)); Mallardo et al. (*Mol. Biol. Cell*, 12:3875-3891 (2001)); Jin et al. (*Cancer Res.*, 63:6154-6157 (2003)); and Vickers et al. (*J. Biol. Chem.*, 278:7108-7118 (2003)). See, Office Action at pages 3-14.

The Final Office Action at page 3 points to Sugiyama et al.'s disclosure of what Sugiyama et al. labels "SEQ ID NO:12." Sugiyama et al.'s SEQ ID NO:12 is a 21-mer DNA sequence, of which nucleotides 2-18 are complementary to the 17-mer SEQ ID NO:1 of the present application. Sugiyama et al. utilized this 21-mer DNA as a RT-PCR primer (see Example 3 and Table 3). The Office Action acknowledges that "Sugiyama et al. do not teach a single-stranded RNA or double-stranded RNA comprising RNA of SEQ ID NO:12."

To remedy this deficiency, the Office Action, at page 4, cites Ast et al., Mallardo et al., Jin et al., and Vickers et al. for their teachings about how to make and use RNA-based antisense oligonucleotides and siRNA compounds.

According to the Final Office Action at page 4,

It would have [been] obvious to one of ordinary skill in the art at the time the invention was made to synthesize an RNA antisense nucleotide molecule of SEQ ID NO:12 of Sugiyama et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success so as to detect/label WT1 in a cell or to use the RNA-based antisense nucleic acid to inhibit the

WT1 expression level at the RNA level, because SEQ ID NO:12 of Sugiyama et al. that is fully complementary to the entire 17-mer SEQ ID NO:1 was known to hybridize specifically with the WT1 nucleotide sequence, and because making and using RNA-based antisense oligonucleotide compounds (including siRNAs) were within the technical grasp of one of ordinary skill in the art at the time the invention was made.

Applicants traverse.

Without in any way acquiescing in this rejection (including the Examiner's response to Applicants' last filed arguments), Applicants have presently amended claim 24 solely with a view towards expediting prosecution of this case. Amended claim 24 is drawn to a composition comprising, as an active ingredient, a single-stranded RNA that consists of a nucleotide sequence that is perfectly complementary to the nucleotide sequence of SEQ ID NO:1. SEQ ID NO:1 is a 17-nucleotide RNA sequence that corresponds to positions 1723-1739 of Wilms' Tumor (WT1) mRNA, *i.e.*, at the 3' end of the WT1 mRNA coding sequence, including two of the three nucleotides of the stop codon. See, page 6, lines 4-11, of the substitute specification filed September 28, 2006.

Applicants note that claim 24 recites that the composition contains "a single stranded RNA that **consists of** a nucleotide sequence that is perfectly complementary to the nucleotide sequence of SEQ ID NO:1." The use of the closed transitional phrase "consists of" indicates that the claimed single-stranded RNA is precisely limited to "a nucleotide sequence that is perfectly complementary to the nucleotide sequence of SEQ ID NO:1." An RNA nucleotide sequence that is perfectly complementary to the nucleotide sequence of SEQ ID NO:1 is:
5' CAAAGGCCAGCUGGAG 3'. Sugiyama et al.'s SEQ ID NO:12 primer, is *longer* than the reference sequence and so includes sequence on both ends that is not complementary to the reference sequence (see comparison of sequences below).

Sugiyama's SEQ ID NO:12: 5' T CAAAGGCCAGCUGGAG TTT 3'

Applicants' Sequence: 5' CAAAGGCCAGCUGGAG 3'

Sugiyama et al.'s SEQ ID NO:12 contains four nucleotides more than permitted by claim 24: three extra nucleotides at one end and one at the other (underlined nucleotides).

There is no disclosure anywhere in any of the cited art, either alone or in combination, of any 17-mer nucleic acid that meets the presently amended language of claim 24. In addition, there would have been no reason apparent to one of ordinary skill in the art to shorten the 21-mer primer DNA disclosed by Sugiyama et al. in such a way so that it exactly meets that limitation.

For at least the reasons discussed above, Applicants submit that claim 24 is not *prima facie* obvious over the cited references, and ask that the rejection over Sugiyama et al. in view of Ast et al., Mallardo et al., Jin et al., and Vickers et al. be withdrawn.

(b) Claim 24 is also rejected as allegedly being obvious over Ware et al. (US 6,232,073 B1) in view of Ast et al. (*supra*); Mallardo et al. (*supra*); Jin et al. (*supra*); and Vickers et al. (*supra*). See, Office Action at pages 14-16.

The Final Office Action at page 14 points to Ware et al.'s disclosure of what Ware et al. labels "SEQ ID NO:30." Ware et al.'s SEQ ID NO:30 is a 21-mer DNA identical to SEQ ID NO:12 of Sugiyama et al., discussed above. Ware et al. utilized this 21-mer DNA as a RT-PCR primer (see item 13 in Table 1). As was the case for the rejection over Sugiyama et al. discussed above, the Office Action, at page 14, acknowledges that "Ware et al. do not teach a single-stranded RNA or double-stranded RNA comprising RNA of SEQ ID NO:30."

The rejection based on Ware et al. combined with Ast et al., Mallardo et al., Jin et al., and Vickers et al. is essentially the same as the rejection based on Sugiyama et al. combined with the same four secondary references. Applicants submit that, for at least the same reasons as outlined above, the rejection over Ware et al. combined with Ast et al., Mallardo et al., Jin et al., and Vickers et al. should not be applied to claim 24, as amended.

Further, the rejection as formulated in the Office action should not be applied to any of the new claims, as all of the new claims either depend from claim 24 or describe the RNA in the same terms as used in claim 24, as amended.

Applicant : Haruo Sugiyama et al.
Serial No. : 10/594,706
Filed : July 30, 2007
Page : 9 of 9

Attorney's Docket No.: 14875-0169US1 / C1-A0402P-US

CONCLUSION

Applicants respectfully submit that the claims under examination are allowable and therefore request the timely issuance of a Notice of Allowability.

The RCE filing fee and the three-month Extension of Time fee in the amount of \$1,110.00 are being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 14875-0169US1.

Respectfully submitted,

Date: August 4, 2011

/Janis K. Fraser/
Janis K. Fraser, Ph.D., J.D.
Reg. No. 34,819

Customer Number 26161
Fish & Richardson P.C.
Telephone: (617) 542-5070
Facsimile: (877) 769-7945

22488512.doc